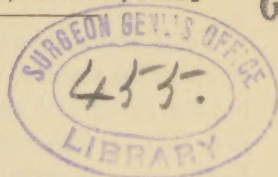


SHURLY (E. L.)

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A STUDY OF THE SPUTUM IN PULMONARY  
CONSUMPTION.

*presented*

By E. L. SHURLY, M.D.,

~~DETROIT, MICH.~~

THE following thoughts and observations are presented as an outline of some work which Dr. Gibbes and myself have undertaken in an endeavor to trace out the pathology and pathological chemistry of so-called tuberculosis.

That the morbid agent is contained in the sputum there is now no doubt, as attested by the numerous instances of its effects in producing the disease in the lower animals by inoculation or insufflation. That its morbid character can, however, be altered or neutralized by several different chemicals outside of the body, and after introduction into the body, we have shown, as attested by the animals now living, which have been subjected to such tests. But just what the particular properties of sputum are, which produce the several varieties of the disease in question in lower animals, we believe is not yet settled, and therefore it is to these questions that I now invite attention.

The prevailing belief is, that, first, bacteria and then bacterial products constitute the principal, if not sole cause of so-called tuberculosis, in all of its varying clinical phenomena. Be this as it may, there is no adequate explanation of the relation of the tissues involved to these things, from any point of view yet given. In other words, we cannot elucidate the first step in the pathogenesis which seems necessary to prepare the way for the action of the bacteria or their products.

The recent labors of Zuegler, Prudden, Buchner, Behring, Roux, Trouessart, McWilliams, and others toward a chemical analysis of the products of microbiosis, especially of the tubercle bacillus, begin to shed some light on the subject, so that we may hope for a solution of the problems in the near future.

Yet it seems to us, that a critical chemical examination, in a comparative manner, of the sputum derived from cases representing the recognized varieties of pulmonary phthisis is a necessary first step of investigation, unless it be admitted that tubercle bacilli not only constitute the sole primary cause of these clinical varieties but also the basis of all further steps of pathogenesis. If this were admitted, then why should A. suffer from laryngeal phthisis, who was never exposed particularly, who never suffered from any sensible throat affection, whose family history and mode of life were excellent; and B. of the same family and whose mode of life was bad, who suffered from abrasions and inflammations of the throat and air passages, and who had been exposed particularly, escape or, perhaps, contract fibroid phthisis later in life? And again, why should C. under similar favorable conditions suffer from acute general tuberculosis; and D. subject to similar environment contract laryngeal phthisis, and so on?

If, therefore, as we have seen, the sputum really contains the *materies morbi*, and if, from our knowledge of the morphology and physiology of the tubercle bacilli, we cannot account for the early phenomena, it becomes incumbent upon us, not only to ascertain, if possible, what these products are, but what their relation is to the tissue change in the first steps of the disease; that is, whether toxic proteids or alkaloids, originating independently of bacteria, by cell- or lymph-necrosis or alteration, play a part in the morbid process, so that we can form a basis for therapeutic action with more or less exactitude.

Hence, the objects of such study would naturally be to ascertain just what the proteids or alkaloids of the sputum are, in the different classes of cases; whether noxious or not, individually; and whether the product of a morbid process, induced or protracted by tubercle bacilli, or independently of them.

The work of Luckjanow "On the General Pathology of the Cell" is highly interesting in this connection as showing the wonderful metamorphosis which these elements undergo through chemical as well as physical action in disease.

The micro-organisms commonly found in the sputum are of great variety; some of which belong particularly to the mouth, while many (such as the bacillus subtilis, bacterium termo, and



micrococcus tetragenus, diplococci, streptococci, staphylococci, pneumococci, and other varieties), have been found in the respiratory passages, and in lung-cavities according to Biondi, Gaffky, David, and others. Although under ordinary conditions saprogenic (Trouessert, Vernueil, Moos, Netler, Zanfai) yet, as suggested by David and Cornil and Babes, any revulsion of the system may render them more or less pathogenic.

The composition of normal sputum, as ordinarily given in the text-books, is as follows: According to Landois and Sterling, it shows microscopically, epithelial cells, and lymphoid cells. The fluid substance of the sputum contains much mucus, together with nuclein, lecithin, and the constituents of saliva.

Under pathological conditions there may be found albumen, red blood corpuscles, pus, elastic fibres, plugs of fibrin, casts of larger or smaller bronchi, crystals of various kinds, fatty acids, and occasionally leucin and tyrosin, Charcot's crystals, hæmoglobin and cholesterin, fungi, and lower organisms taken in during respiration, threads of leptothrix, mycelium, and spores of oidium albicans, various rod-shaped bacteria, monads, and cercomonads.

We are investigating now the sputum obtained from several different cases of pulmonary phthisis, all of which are quite advanced.

Case B.—General tuberculosis.

Case H.—Acute miliary tuberculosis.

Case K.—Chronic fibroid phthisis.

Case D.—Sub-acute phthisis.

Case C.—Ordinary chronic phthisis with large excavation, the case now being under treatment.

Two lines of procedure are in progress: First, by cultivation of the microbes in different media under different conditions; and second, chemical examination, and the inoculation of the several derived products in mice, guinea-pigs, and rabbits. As mentioned before, the work is too incomplete to draw definite conclusions, but a few results have been obtained which may be interesting. Our chemical procedure in the main is something as follows: The sputum is collected in the morning, after the patient's mouth has been washed out with a solution of salt and water. In all instances

it is first either boiled from one to two hours, or heated at a high temperature in a culture-oven, having been mixed with either distilled water, alcohol, solution of sodium hydrate, hydrochloric acid, or saturated solution of sodium chloride, in equal proportions. Concerning mucin, we find that it varies very much in its reactions according to the specimen. From several specimens we were unable to separate any at all. We thoroughly believe with Lowenberg that mucin varies in its nature according to the animal or substance from which it is obtained.

H—sputum. Four ounces of this was diluted with an equal part of water, and two drachms of sodium hydrate were added; it was then boiled with an inverted condenser for two hours over a sand-bath and filtered. The clear filtrate gave the following reactions:—

| <i>Reagents.</i>           | <i>Precipitates.</i> |
|----------------------------|----------------------|
| Alcohol . . . . .          | Faint white.         |
| Ammonium chloride . . . .  | White.               |
| “ hydrate . . . . .        | None.                |
| Silver nitrate . . . . .   | A dirty brown.       |
| Barium chloride . . . . .  | White.               |
| “ hydrate . . . . .        | Brown.               |
| “ nitrate . . . . .        | White.               |
| Calcium chloride . . . . . | “                    |
| Copper sulphate . . . . .  | Blue.                |

Part of the original filtrate was acidified with acetic acid, and lead acetate was added in excess. The resulting white precipitate was filtered off, and hydrogen sulphide was passed through the filtrate to remove the lead. After standing in a test tube plugged with cotton, and after the precipitated sulphur had been removed, the extract thus freed of mucin, which was acid, gave the following reactions:—

| <i>Reagents.</i>               | <i>Precipitates.</i> |
|--------------------------------|----------------------|
| Lead acetate . . . . .         | None.                |
| Gold chloride . . . . .        | “                    |
| Potassio-mercuric-iodide . . . | “                    |
| Phospho-molybdic acid . . .    | “                    |
| Phospho-tungstic acid . . .    | White.               |
| Sulpho-salicylic acid . . . .  | None.                |

The precipitate obtained with phospho-tungstic acid was washed and desiccated over sulphuric acid.

The whitish residue was stirred up with a little distilled water, and five minims were injected into a mouse. The animal was sick for a week, and after several weeks escaped.

A portion of the original filtrate was placed in a test-tube and carbonic acid gas was passed through it for twenty-four hours; this was then allowed to stand for two weeks. A white precipitate gradually formed. The supernatant fluid was decanted off and treated as follows:—

| <i>Reagents.</i>      |       | <i>Precipitates.</i> |
|-----------------------|-------|----------------------|
| Phospho-molybdic acid | . . . | White.               |
| Phospho-tungstic acid | . . . | "                    |
| Tartaric acid         | . . . | "                    |
| Lead acetate          | . . . | "                    |

Five minims of this supernatant fluid were injected into a mouse. The animal lived twenty-two days (the same number of days that the animal lived that was injected with the glycerine extract of the B—sputum). The post-mortem examination showed a general softening of the tissues.

C—sputum. Four ounces were treated with an equal quantity of a strong solution of tartaric acid, shaken at intervals during an hour, and filtered. The clear filtrate gave the following reactions:—

| <i>Reagents.</i>       |       | <i>Precipitates.</i>   |
|------------------------|-------|------------------------|
| Phospho-molybdic acid  | . . . | White.                 |
| Gold chloride          | . . . | None.                  |
| Sulpho-salicylic acid  | . . . | White.                 |
| Phospho-tungstic acid  | . . . | "                      |
| Lead acetate           | . . . | Dense white.           |
| Ferric chloride        | . . . | None.                  |
| Potassium ferricyanide | . . . | Green.                 |
| " bichromate           | . . . | Red.                   |
| " ferrocyanide         | . . . | White.                 |
| Tannic acid            | . . . | Dense greenish-yellow. |

Two and a-half grains of the phospho-tungstic precipitate were rubbed up with fifteen minims of pure glycerine, and three minims of this mixture injected into a mouse. The mouse died after three



days. A like solution of phospho-tungstic acid did not kill the control mouse.

Four ounces of the sputum were treated with eight ounces of water and thirty grains of citric acid, shaken frequently for an hour and filtered. This gave the following reactions:—

| <i>Reagents.</i>          | <i>Precipitates.</i> |
|---------------------------|----------------------|
| Lead acetate . . . .      | None.                |
| Hydrochloric acid . . . . | “                    |
| Nitric acid . . . .       | “                    |
| Platinic chloride . . . . | “                    |
| Mercuric chloride . . . . | “                    |
| Tannic acid . . . .       | Slight gray          |

This shows entire absence of albumens. The gray precipitate may have been due to a trace of iron. Twenty-five minims injected into a rabbit failed to produce death, as also twenty-five minims, injected into another rabbit, of the filtrate procured from the tartaric sputum. Two ounces of sputum were treated with an equal quantity of alcohol, heated gently over a water-bath for fifteen minutes, and filtered; lead acetate was added, hydrogen sulphide passed through, filtered into a test-tube plugged with cotton, and allowed to stand two weeks. This gave the following reactions:—

| <i>Reagents.</i>                 | <i>Precipitates.</i> |
|----------------------------------|----------------------|
| Lead acetate . . . .             | None.                |
| Gold chloride . . . .            | Brownish-black.      |
| Sulpho-salicylic acid . . . .    | None.                |
| Potassio-mercuric-iodide . . . . | “                    |
| Phospho-tungstic acid . . . .    | White.               |
| Phospho-molybdic acid . . . .    | “                    |

Five minims of this alcoholic extract (mucin free) were injected into a mouse. The animal died in fifteen days. The precipitate with phospho-molybdic acid was stirred up with distilled water, and five minims were injected into a mouse. The animal had a convulsive chill lasting until death, which occurred after eight hours. The control mouse did not die.

A quantity of sputum was boiled with an equal bulk of water strongly acidulated with hydrochloric acid, and filtered. The clear filtrate gave the following reactions:—

| <i>Reagents.</i>         |       | <i>Precipitates.</i> |
|--------------------------|-------|----------------------|
| Phospho-molybdic acid    | . .   | White.               |
| Gold chloride            | . . . | Yellow.              |
| Sulpho-salicylic acid    | . .   | White.               |
| Potassio-mercuric-iodide | . .   | "                    |

This last precipitate was thoroughly washed and allowed to settle. The heavy flaky mass was soluble in boiling nitric acid, but not in cold acid; soluble in cold hydrochloric acid. Heated with sulphuric acid a rose-colored opaque solution resulted. The precipitate was soluble in ammonium hydrate, insoluble in ether, readily soluble in ammonium sulphide. Solutions of this precipitate in ammonium sulphide, when injected into mice, caused speedy death; however, the control mice, injected with the ammonium sulphide alone, died in a short time also. We are now engaged in trying these solutions upon larger animals which do not succumb to the ammonium sulphide. Fifteen minims of a solution of this precipitate in ammonium sulphide, when injected into a guinea-pig, produced constitutional disturbances characterized by swelling of the glands of the neck, which diminished after two or three days. The precipitate, when rubbed upon an abraded surface of a rabbit's ear, produced an intense local inflammation lasting for several days. Nevertheless, the animal seemed to recover soon from any general illness. When the precipitate was treated with alcohol, it was found that a portion of it was dissolved; the alcohol was then decanted off and evaporated until a grayish powder remained. A ten per cent. solution of this powder (in glycerine) injected into a mouse caused death in ten minutes. A quantity of this same sputum was treated with an equal bulk of alcohol acidulated with acetic acid, boiled and filtered.

This gave the following reactions:—

| <i>Reagents.</i>         |       | <i>Precipitates.</i> |
|--------------------------|-------|----------------------|
| Phospho-tungstic acid    | . .   | White.               |
| Phospho-molybdic acid    | . .   | "                    |
| Gold chloride            | . . . | Yellow.              |
| Potassio-mercuric-iodide | . .   | White.               |
| Sulpho-salicylic acid    | . .   | "                    |

D—sputum. This was diluted with an equal volume of distilled water, and kept at 99° F. for twelve hours, and filtered

three times (it gave a slightly acid reaction). This preparation produced the following reactions :—

| <i>Reagents.</i>                 | <i>Precipitates.</i>          |
|----------------------------------|-------------------------------|
| Nitric acid . . . .              | White ring.                   |
| Lead acetate . . . .             | “                             |
| Hydrochloric acid . . . .        | None (cloudy after standing). |
| Ammonium carbonate . . . .       | “                             |
| “ chloride . . . .               | “                             |
| “ hydrate . . . .                | “                             |
| “ oxalate . . . .                | Slightly cloudy.              |
| Silver nitrate . . . .           | Slightly yellow.              |
| Barium chloride . . . .          | None.                         |
| “ hydrate . . . .                | White.                        |
| “ nitrate . . . .                | None.                         |
| Calcium chloride . . . .         | “                             |
| Copper sulphate . . . .          | “                             |
| Ferric chloride . . . .          | “                             |
| Ferrous sulphate . . . .         | Cloudy.                       |
| Platinum chloride . . . .        | “                             |
| Ammonium sulphide . . . .        | None.                         |
| Hydrogen sulphide . . . .        | “                             |
| Acetic acid . . . .              | Slight.                       |
| Potassium ferrocyanide . . . .   | None.                         |
| “ ferricyanide . . . .           | Very slight.                  |
| “ iodide . . . .                 | None.                         |
| “ carbonate . . . .              | “                             |
| “ hydrate . . . .                | Very slight.                  |
| Gold chloride . . . .            | None.                         |
| Tartaric acid . . . .            | White.                        |
| Potassio-mercuric-iodide . . . . | “                             |
| Formic acid . . . .              | “                             |
| Phospho-molybdic acid . . . .    | Blue.                         |

We failed to produce any alkaloidal crystals from any of these precipitates.

D—sputum. An extract of this sputum was made with hydrochloric acid, and diluted one-half. Of this five minims were injected into a mouse, which died on the eighth day, having shown severe constitutional disturbance.

K—sputum. This was diluted with an equal volume of distilled water, and boiled for four hours with an inverted condenser over a sand-bath and filtered, and the filtrate labelled A-1. To the residue on the filter-paper a saturated solution of potassium



carbonate was added and allowed to pass through. This filtrate was labelled A-2. Alcohol was then added to the residue on the filter-paper and filtered. This filtrate was labelled A-3. Ether was added to what still remained on the filter-paper, and this filtrate labelled A-4.

A-1 was a milky fluid alkaline in reaction, and contained sugar by Fehling's test. Boiled with nitric acid it became clearer.

A-1 gave the following reactions :—

| <i>Reagents.</i>                | <i>Precipitates.</i> |
|---------------------------------|----------------------|
| Platinum chloride . . .         | None.                |
| Mercuric chloride . . .         | "                    |
| Hydrochloric acid . . .         | "                    |
| Nitric acid . . .               | "                    |
| Copper sulphate . . .           | "                    |
| Boiled with potassium hydrate . | White flocculent.    |
| Lead acetate . . .              | White.               |
| Silver nitrate . . .            | Slight white.        |
| Ammonium oxalate . . .          | White.               |
| Gold chloride . . .             | None.                |

The precipitate obtained with potassium hydrate and heat was filtered and the residuum washed, dessicated, and a five per cent. solution was made in water. Of this solution five minims were injected into a mouse. The animal died seven days afterward. No alteration of tissues noted on post-mortem examination.

A-3 gave the following reactions :—

| <i>Reagents.</i>          | <i>Precipitates.</i> |
|---------------------------|----------------------|
| Tannic acid . . .         | Dense gray.          |
| Phospho-molybdic acid . . | Slight white.        |
| Phospho-tungstic acid . . | Dense white.         |
| Acetic acid . . .         | None.                |

Five drops of the A-3 solution injected into a mouse caused the animal's death in an hour.

B—sputum. This was diluted with an equal part of glycerine heated over a water-bath for half an hour, and then filtered by means of an exhaust pump through a plaster plug in the funnel. Three minims of this injected into a mouse caused death in twenty-two days. Post-mortem examination revealed a general softening of the tissues, but no particular local change.

Another portion was treated with water and ether, shaken thoroughly, and allowed to settle. The ether was then removed by means of a separating funnel, alcohol was added to the residue, and separated. The ether extract failed to show any reaction with any reagents at our disposal; and, when allowed to evaporate, left a scarcely perceptible deposit. The alcoholic extract failed to respond to all reagents used excepting tannic acid. From this we may conclude that heat is necessary in the process of chemical separation.

It may be asked what these precipitates are: whether acid albumen, alkali albumens, alkaloids, etc. We can only reply that we have been unable in many instances to obtain satisfactory results, although following closely processes published by well-known chemists. Mr. P. M. Hickey, also our assistant at the Harper Hospital Laboratory, who is a diligent scientific man and a good chemist, has spent much time and thought, especially in this direction, without being able to identify and classify many of the products thrown out.

We hope soon to be able to show some of the ulterior pathological results in guinea-pigs, rabbits, and monkeys, from the inoculation of the elements of the sputum under consideration. We hope also to learn the effects of so-called bacteria proteids on organic substances, and on the lower animals; and, finally, if practicable, to work out some systematic method for their neutralization in the body.

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### DISCUSSION.

J. H. TYNDALE, M.D. I have heretofore had explained to me the results of the labors of Dr. Shurly and his coadjutor, and hope that hereafter their labors will result in something more tangible.

ALBERT L. GIHON, M.D., U.S.N. I do not desire to discuss the matter, but would like to make the suggestion to Dr. Shurly that he continue his investigations and that in the paper which we hope he will give us next year he may suggest some practical

way of getting rid of this dangerous sputum being scattered all around. Last December I went to Charleston on board a steamer on which there were some thirty consumptives on their way to Florida, many of whom insisted upon having every window and door in the cabin shut, and all the fires going, and they were expectorating in every direction, soiling carpets, cushions, curtains, and the bedding of their own state-rooms. There was, accordingly, great danger to those of us who had receptive lungs. In the naval hospital of which I have charge, it is easy for me to compel the patients to use the paper spit-cup. I say it is easy—but not so very easy after all, for though when they expectorate in their own wards and under supervision of the nurses I can compel them to use the paper cup, they are less careful about doing so on the corridors and stairways. The majority, however, get so that they will, if they can avoid it, not expectorate, and so contract the habit of swallowing the sputum. So it seems to me that if I could not wholly compel the use of paper spit-cups in a military hospital, it would certainly be very difficult in civil life to prevent people from ejecting sputum in steam-cars and steam-boats, which are often overheated, especially those which carry invalids.

So far as there shall be any possible way of disposing of sputum with proper regard to sanitary conditions Dr. Shurly should be the man to discover it by his investigations, and give us the result in his next paper.

H. F. WILLIAMS, M.D. I was specially interested with Dr. Shurly's account of his labors. I believe it quite probable that further biological research will discover a great deal of difference in the strength and innocuousness of the bacilli, dependent upon the number of removes from the primary culture of each colony. I do not see how it is possible to explain the violence of the symptoms which exhibit themselves in certain cases without any proportionate lesion except on the ground of violence in the germ itself. I believe one section of Dr. Shurly's paper referred to that.



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